

Combinatorial compound library

- 15,000 compounds screened; collection growing
- Novel “drug like” molecules by Lipinski’s “rule of 5”
- Based on 125 templates, 200 congeners each

BEST AVAILABLE COPY

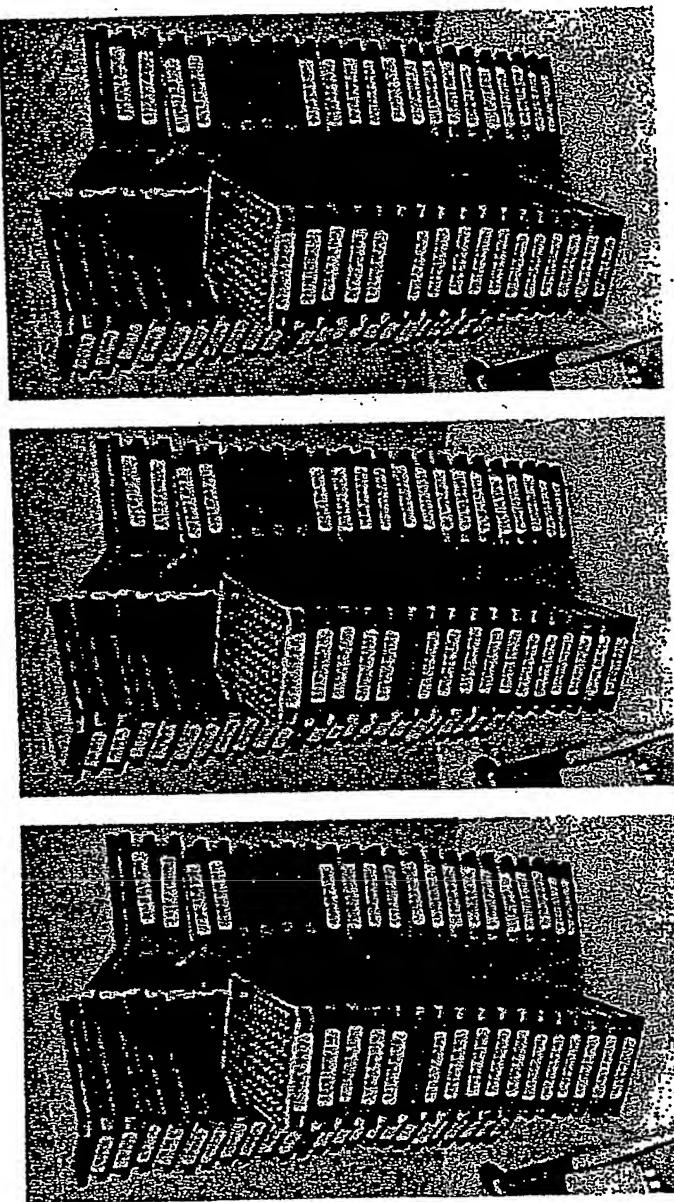
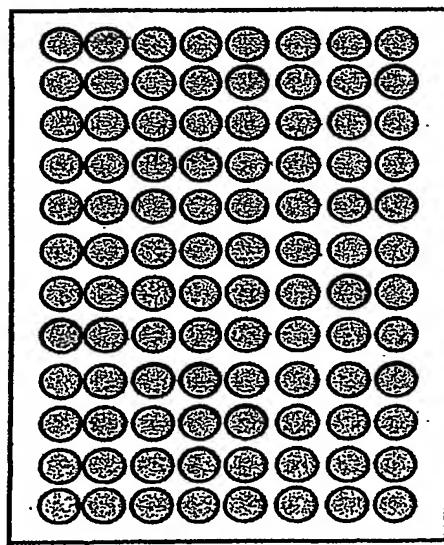


Figure 1

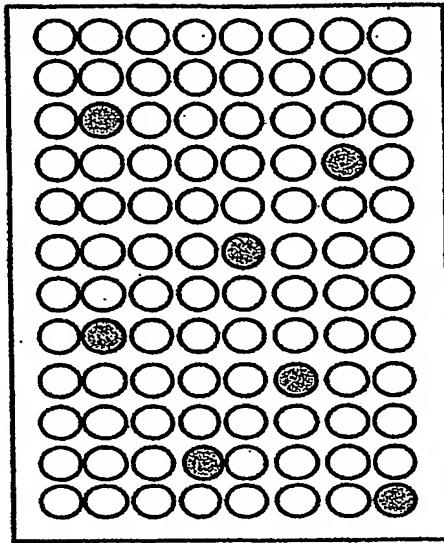
Screening scheme

assay mix/compound/mix

(T90)



90 min at 37°C



1.5×10^4 neutrophils/well
incubate with test agents
37°C for 30 min; add TNF

Inhibitors of TNF specific
signaling molecules

Toxicity to neutrophils[]

Inhibitors of the assay itself (HRP)
Intrinsic fluorescence

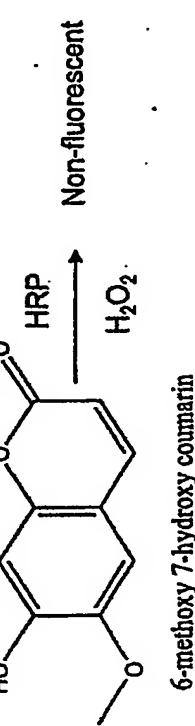


Figure 2

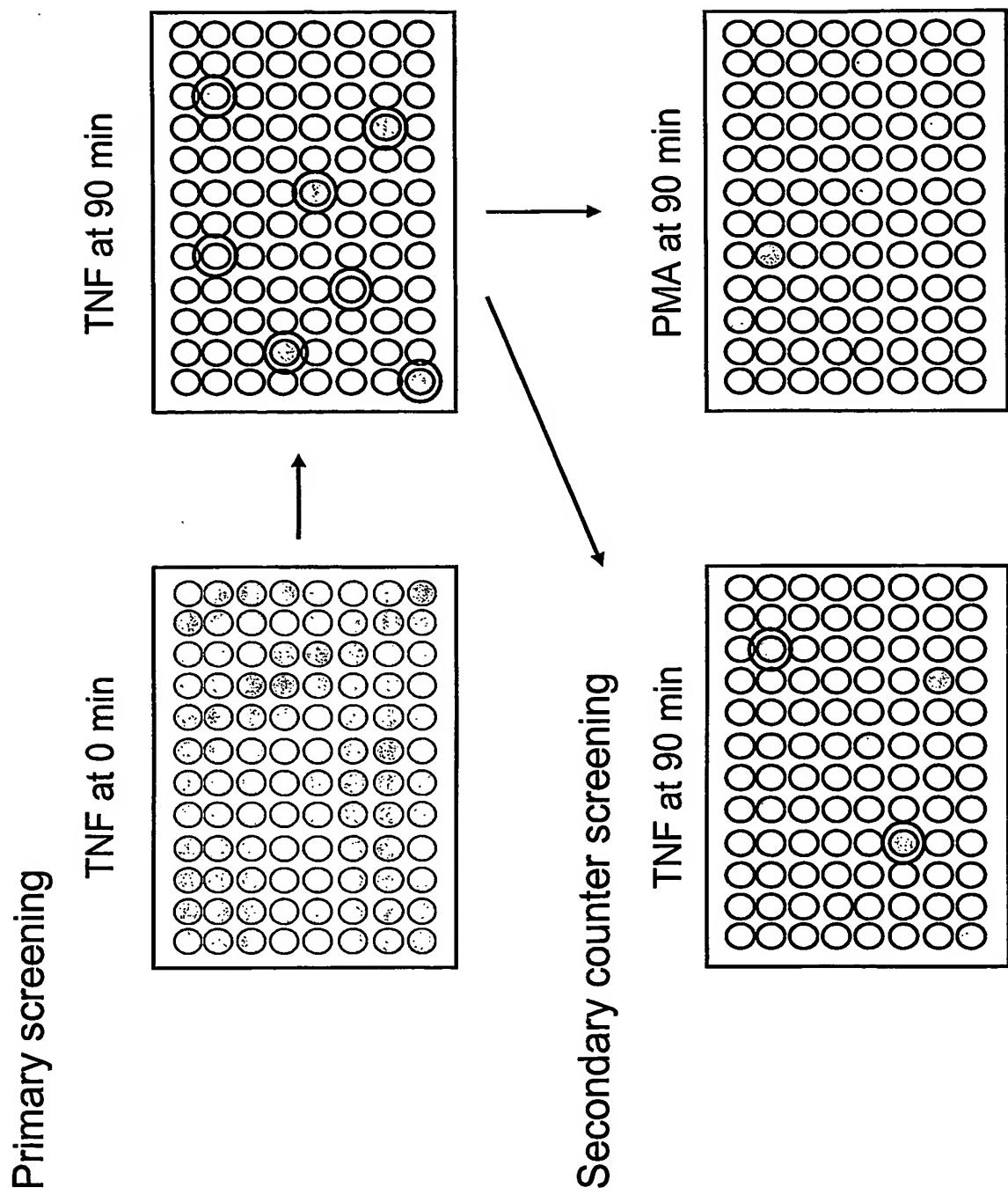
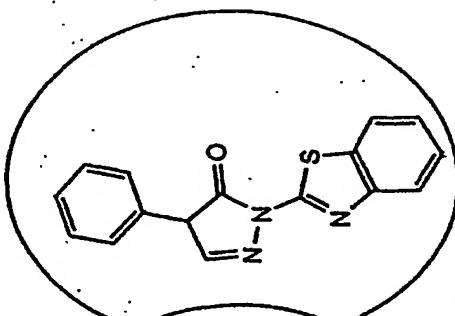
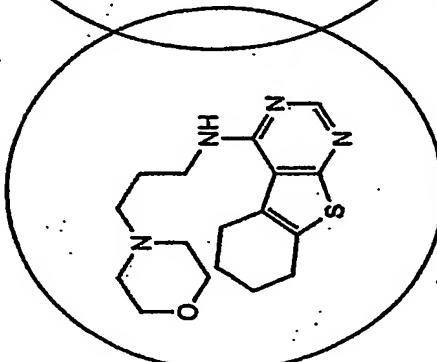


Figure 3

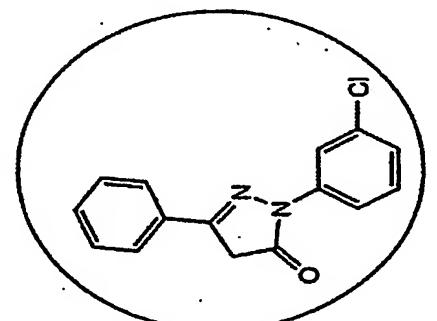
Inactive controls



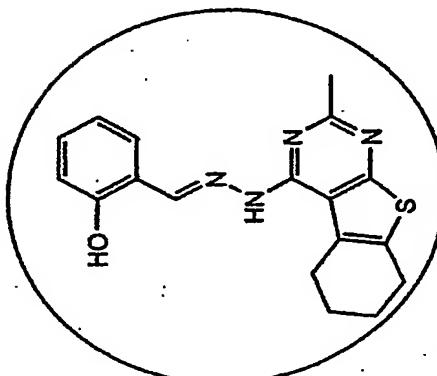
49G04 (CL0651) 37A03 (CL0326)



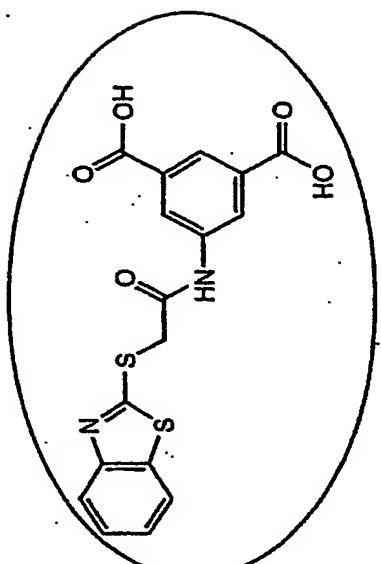
Active inhibitors



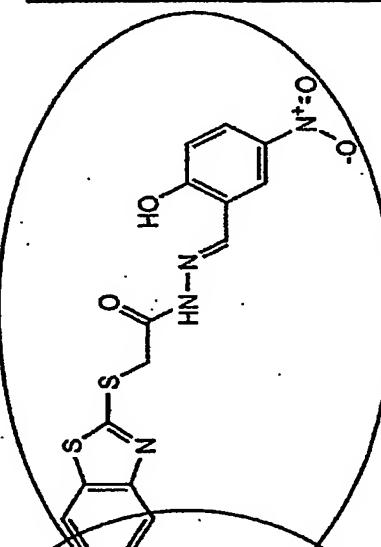
53F03 (CL0326)



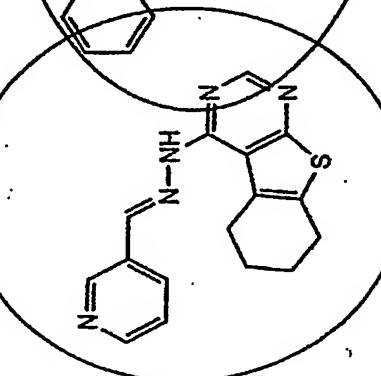
23G01 (CL0651)



120A07 (CL0338)



109G01 (CL0338)



55D01 (CL0651)

Figure 4

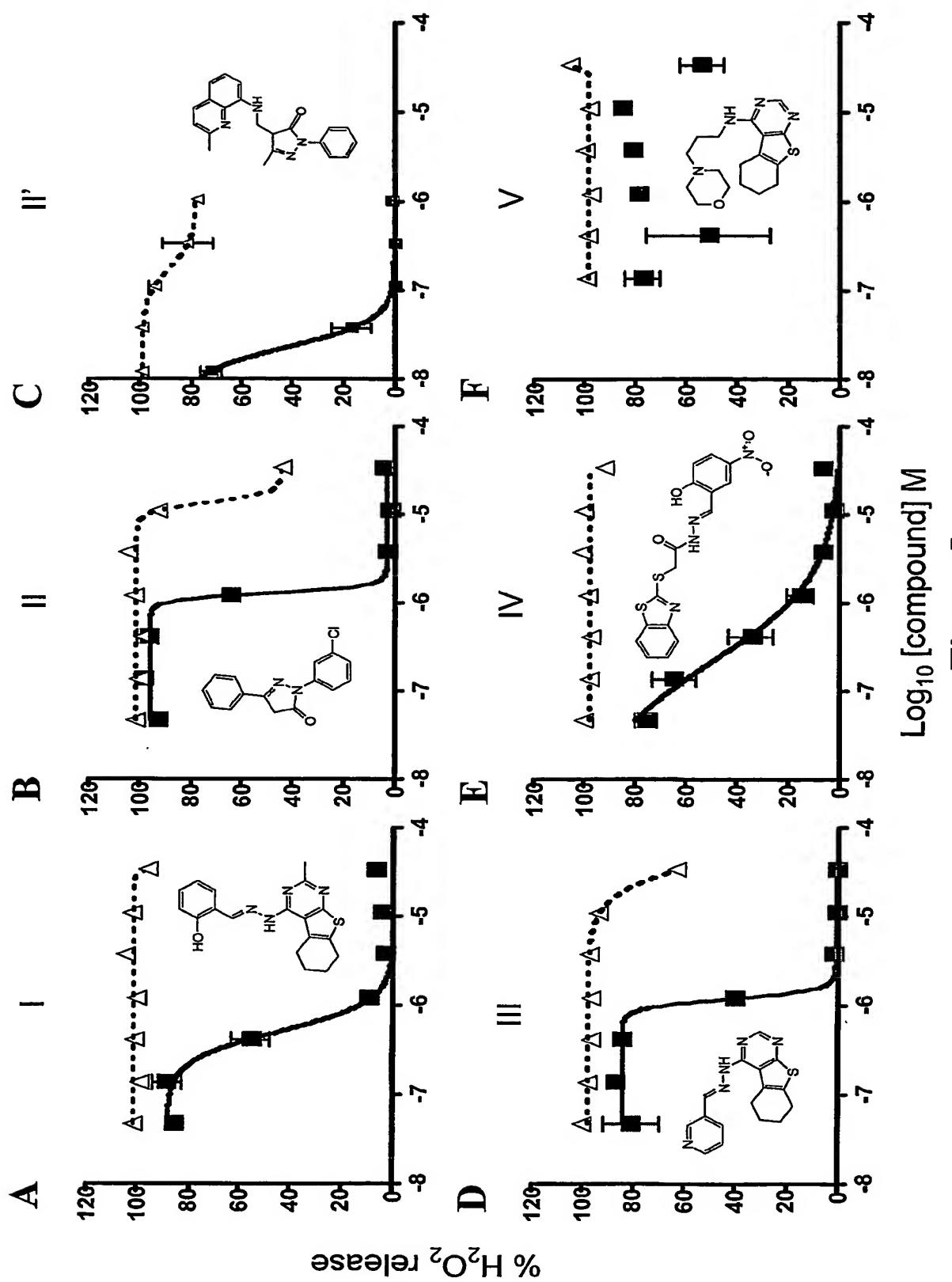


Figure 5

Log₁₀ [compound] M

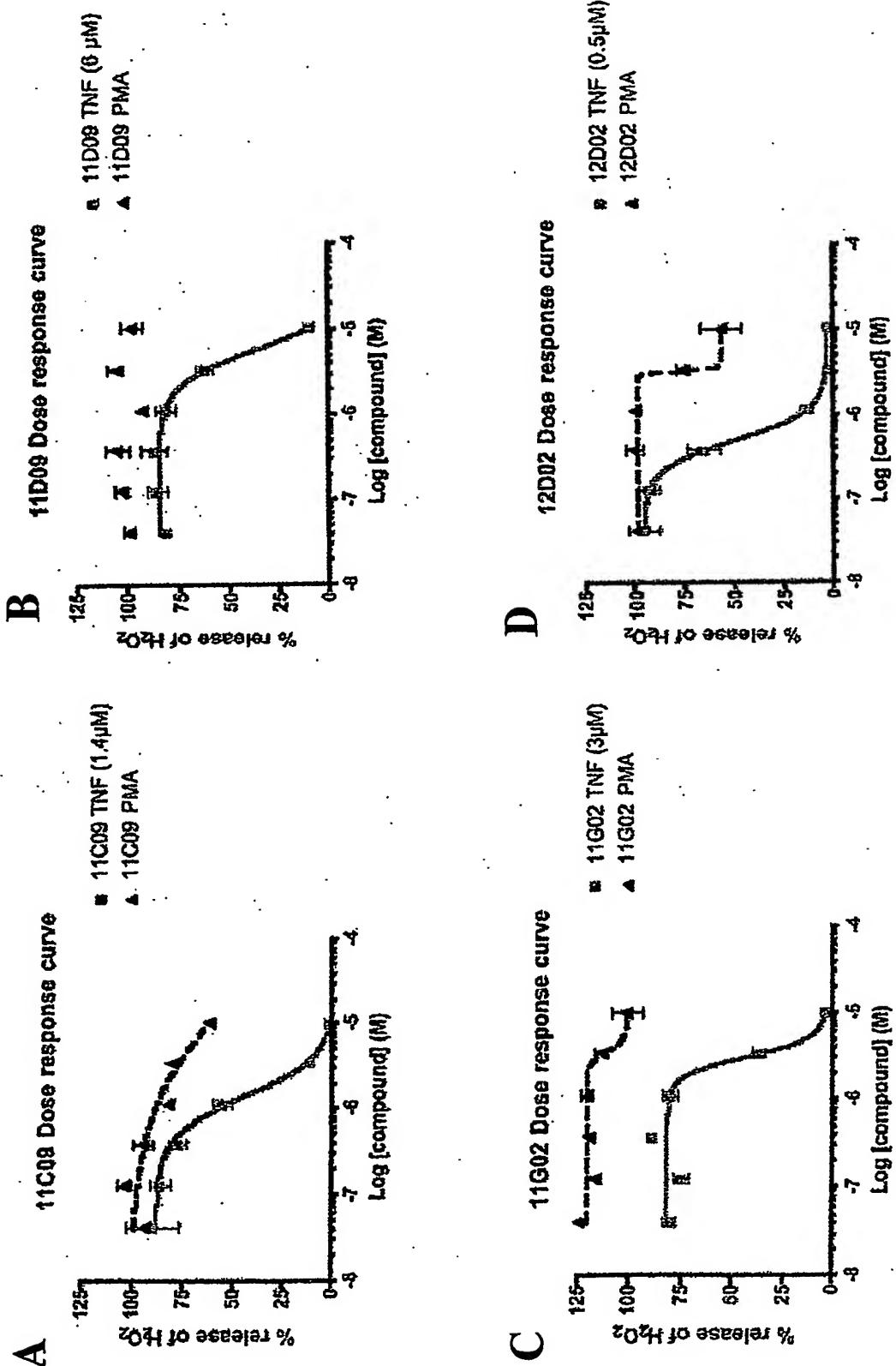


Figure 6

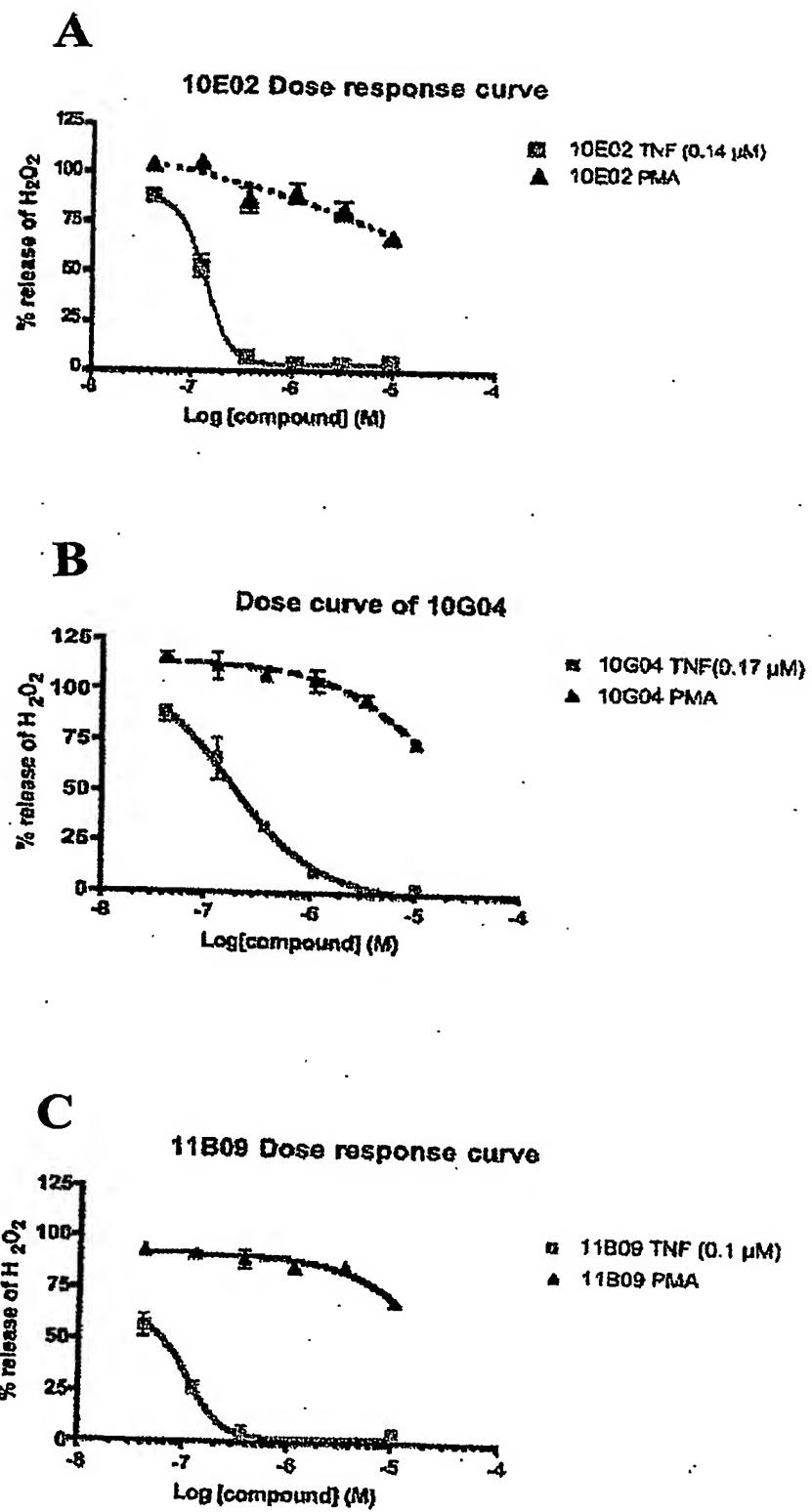


Figure 7

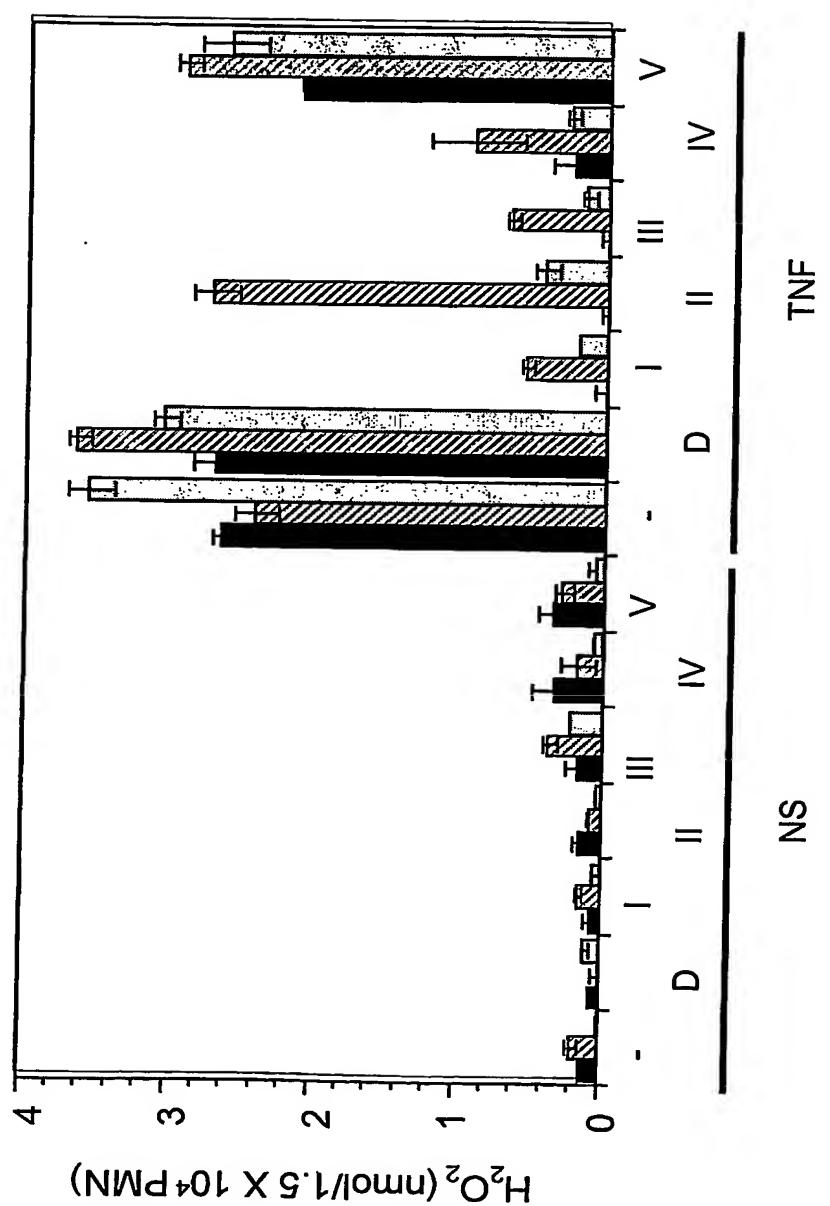


Figure 8

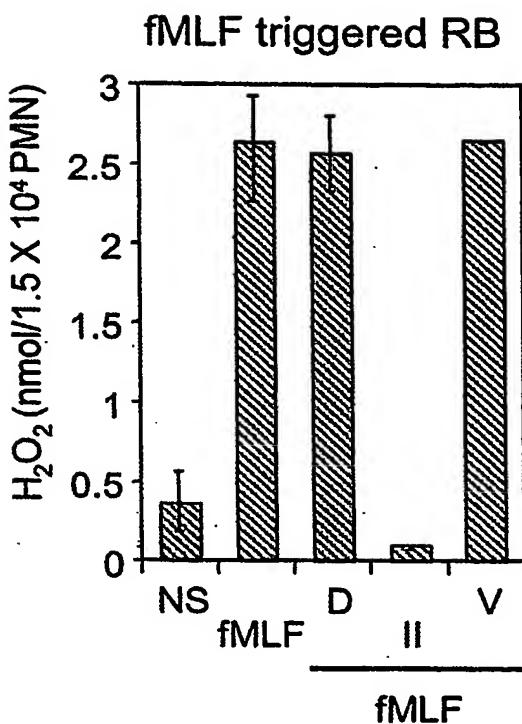


Figure 9A

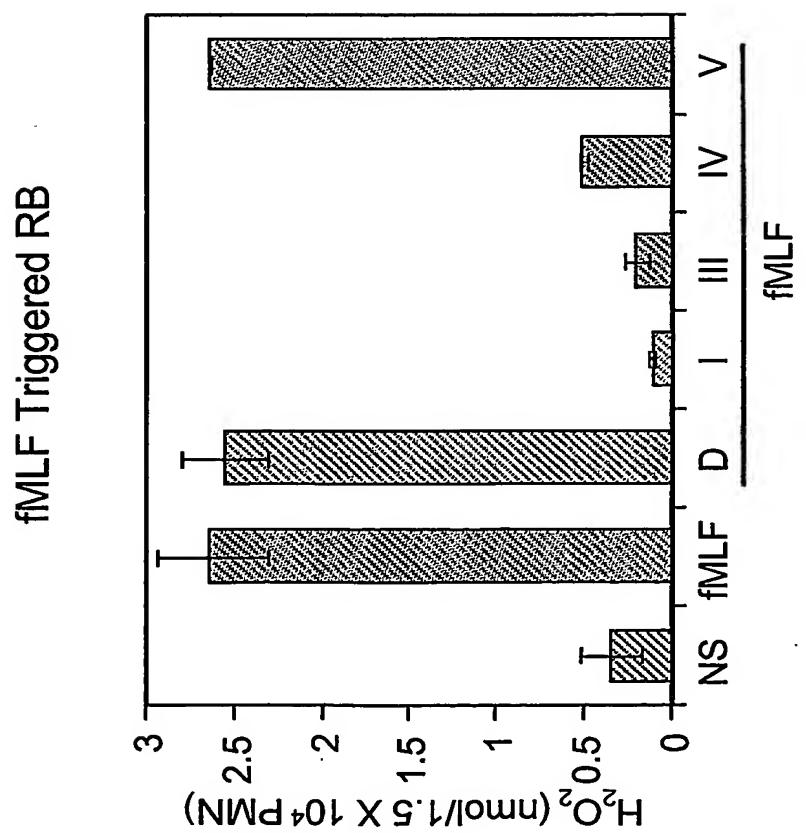


Figure 9 B

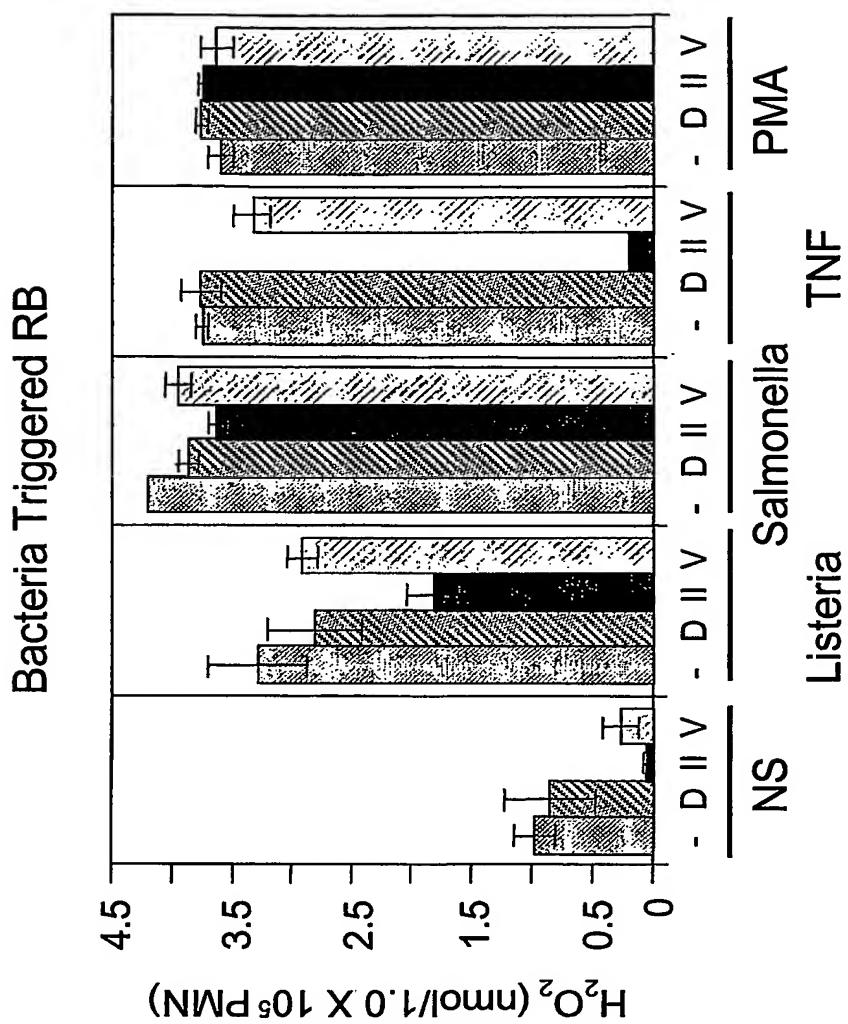


Figure 10A

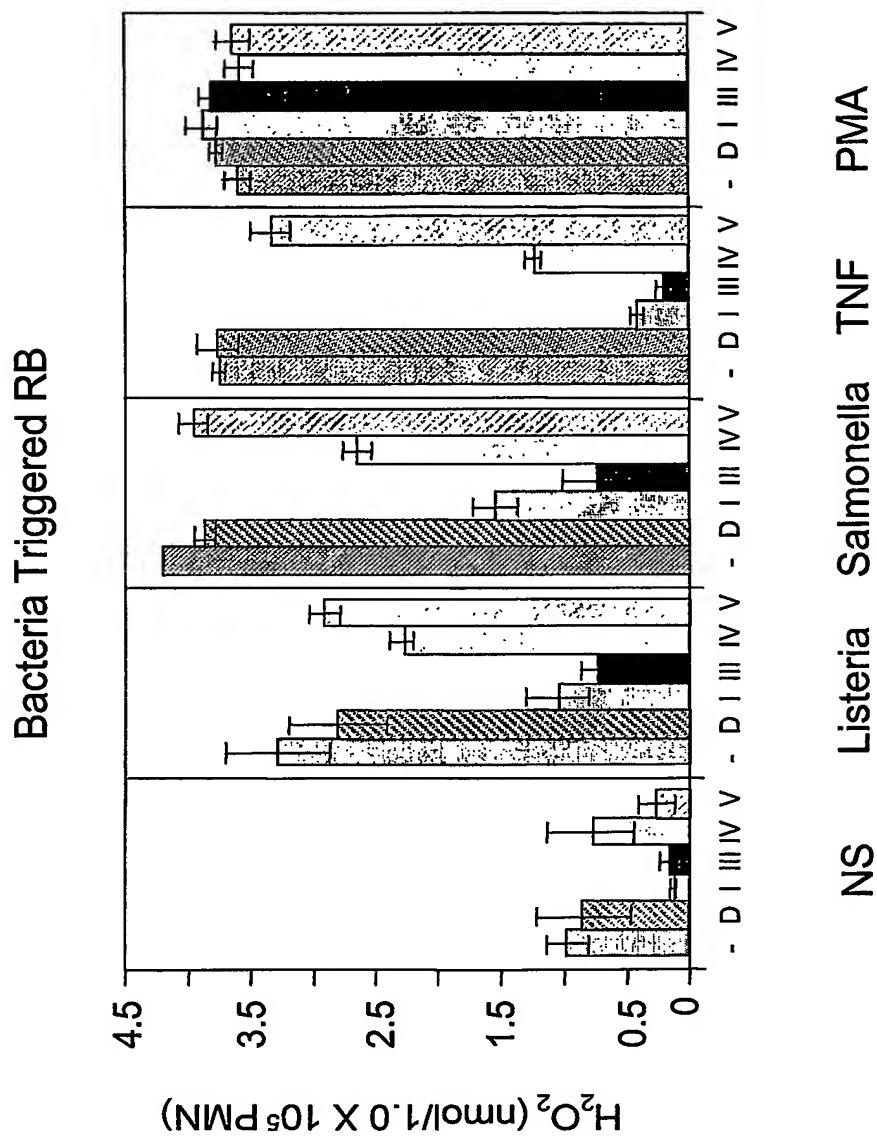


Figure 10B

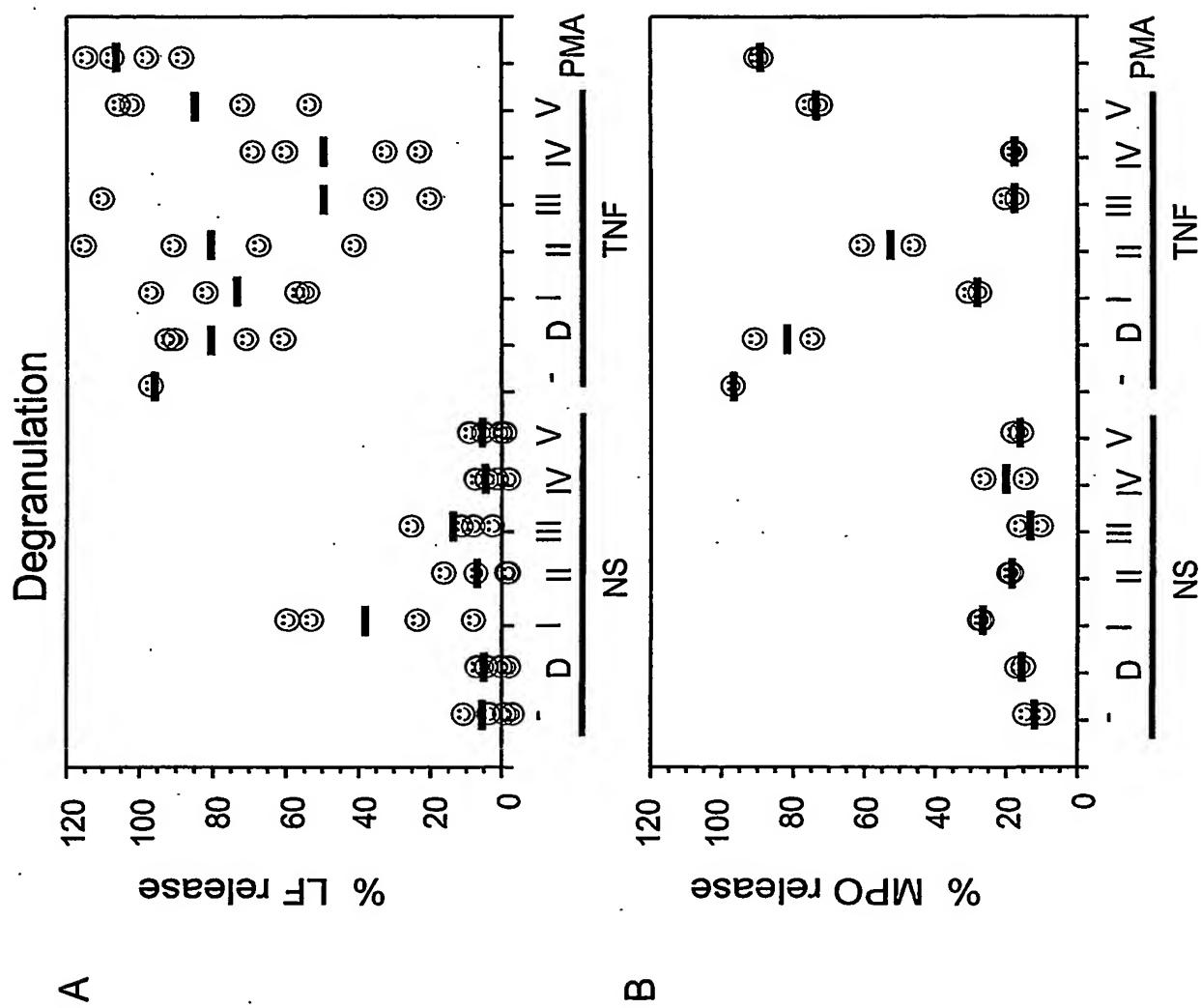


Figure 11

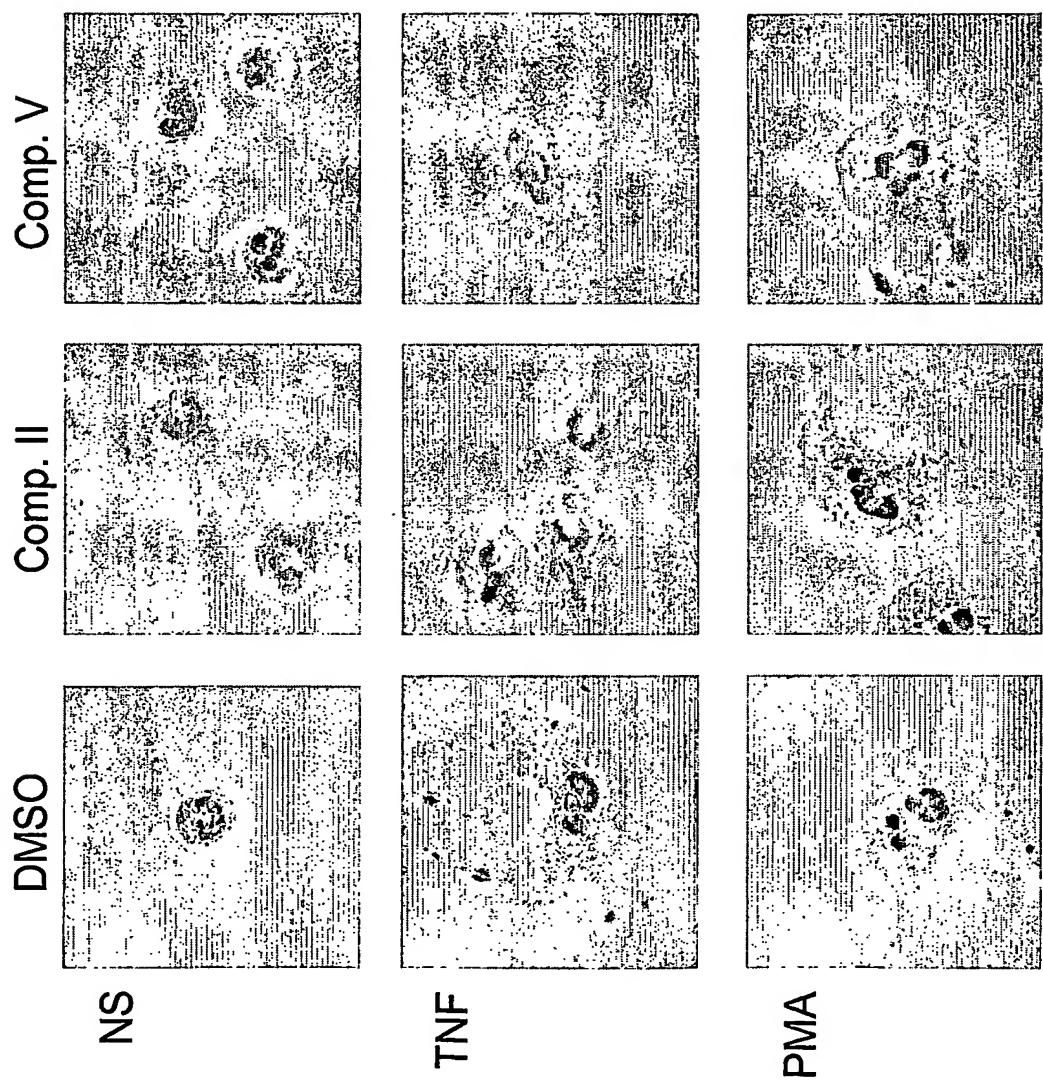


Figure 12A

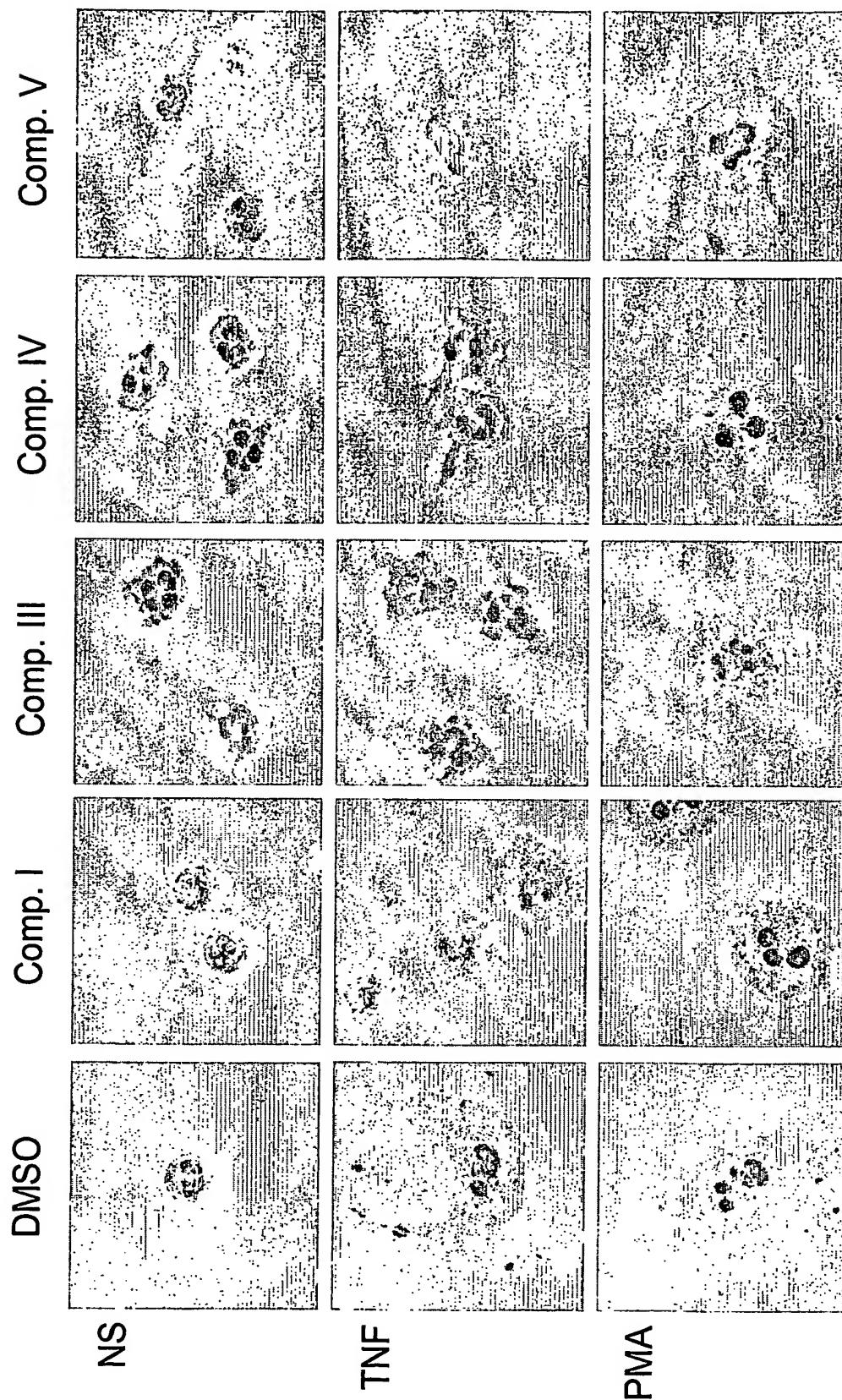
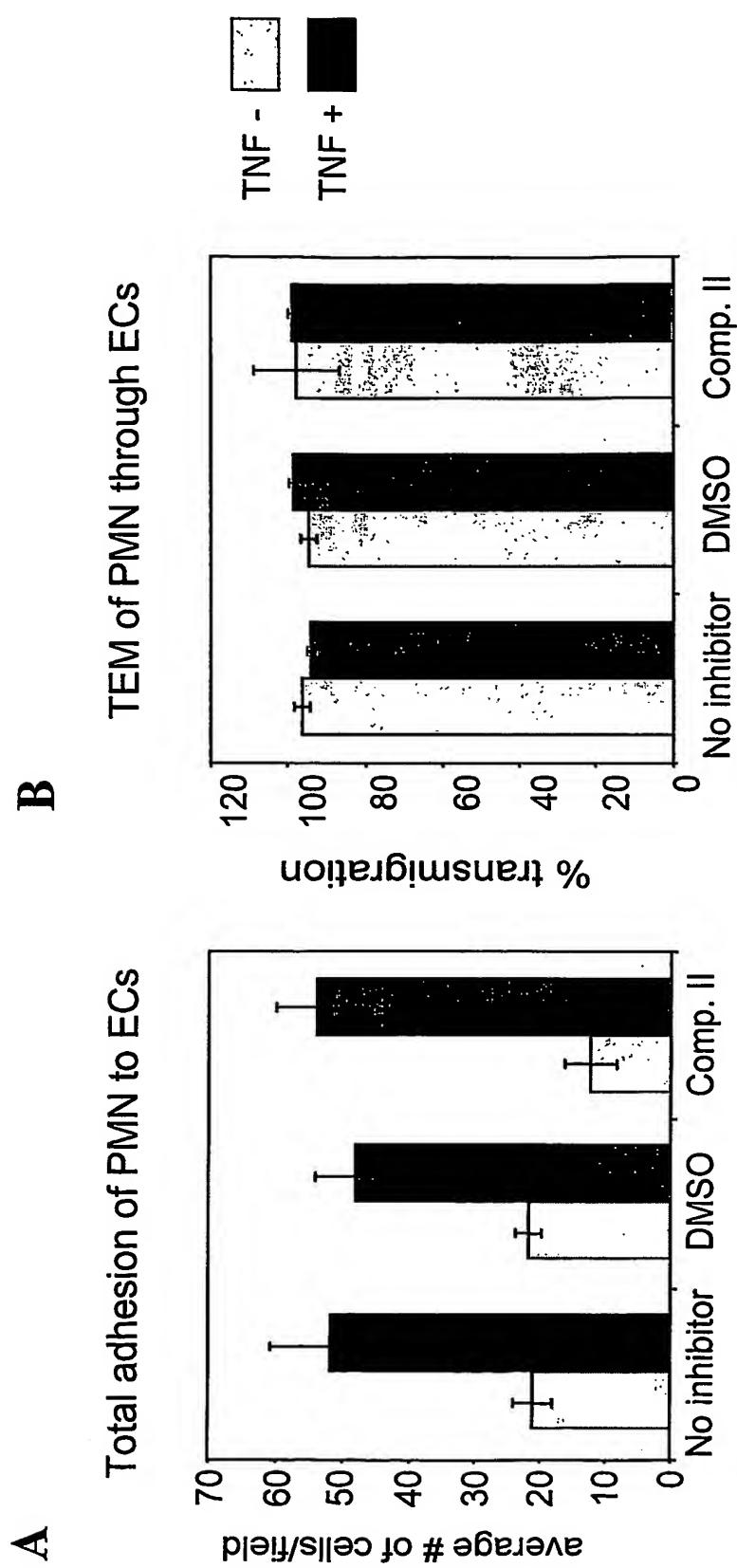


Figure 12B

**Figure 13**

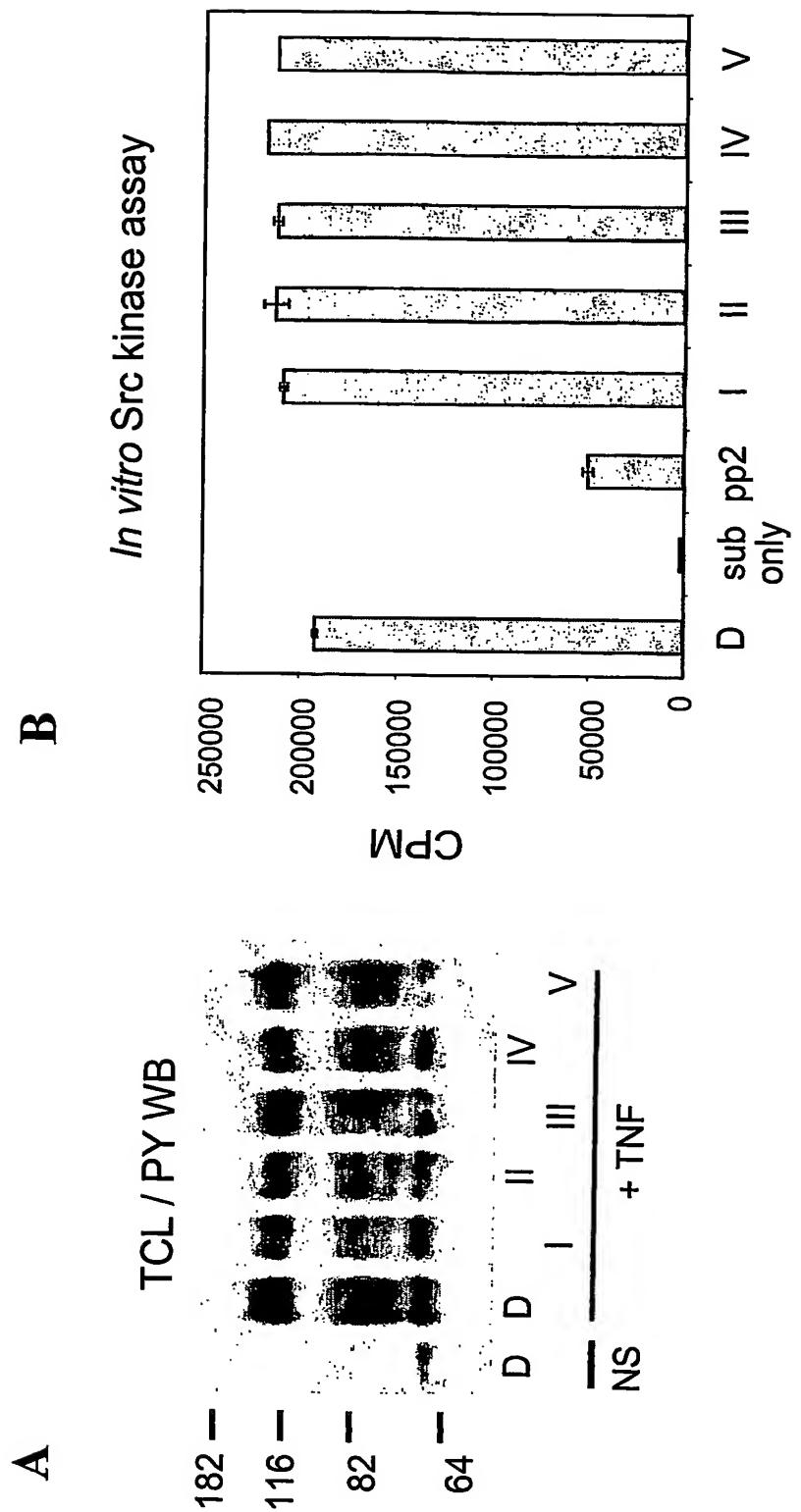


Figure 14A-B

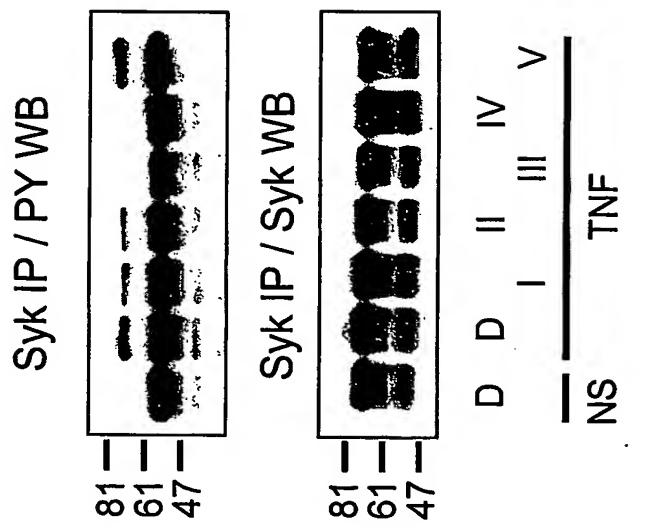


Figure 14C

In vitro Syk Kinase Assay

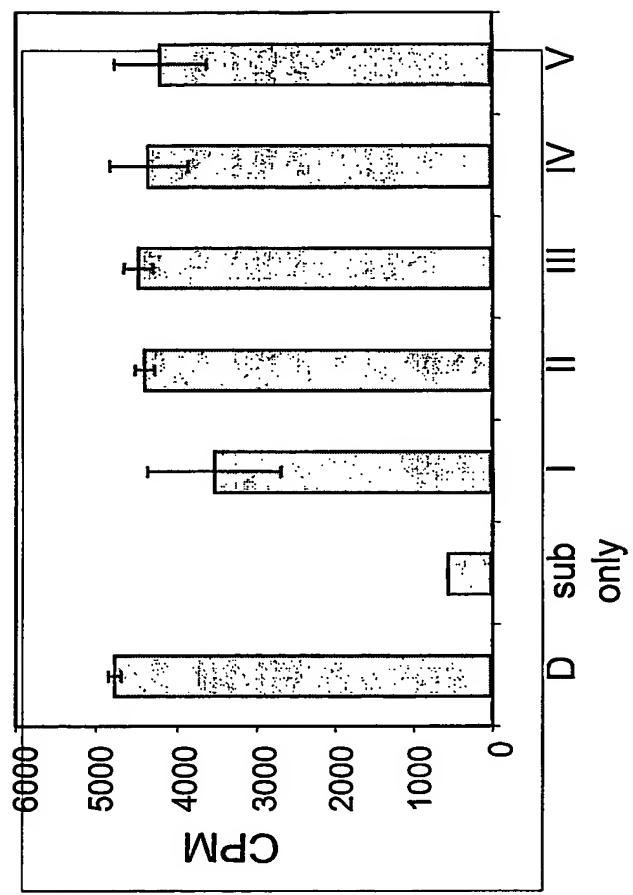


Figure 14D

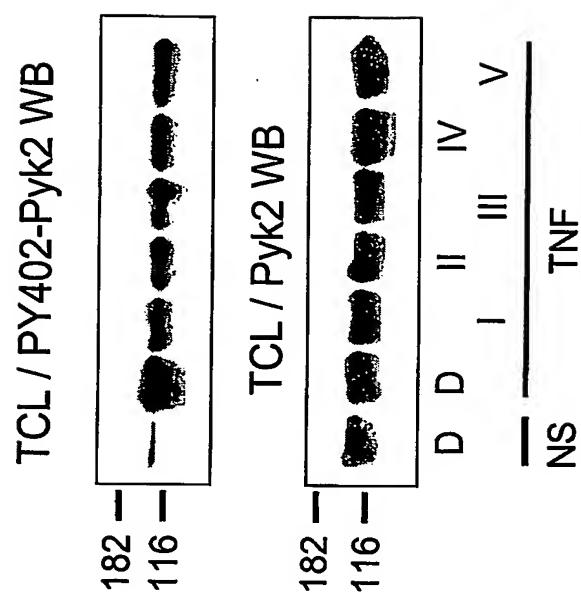


Figure 15

Phagocyte oxidase (phox) (NADPH oxidase)

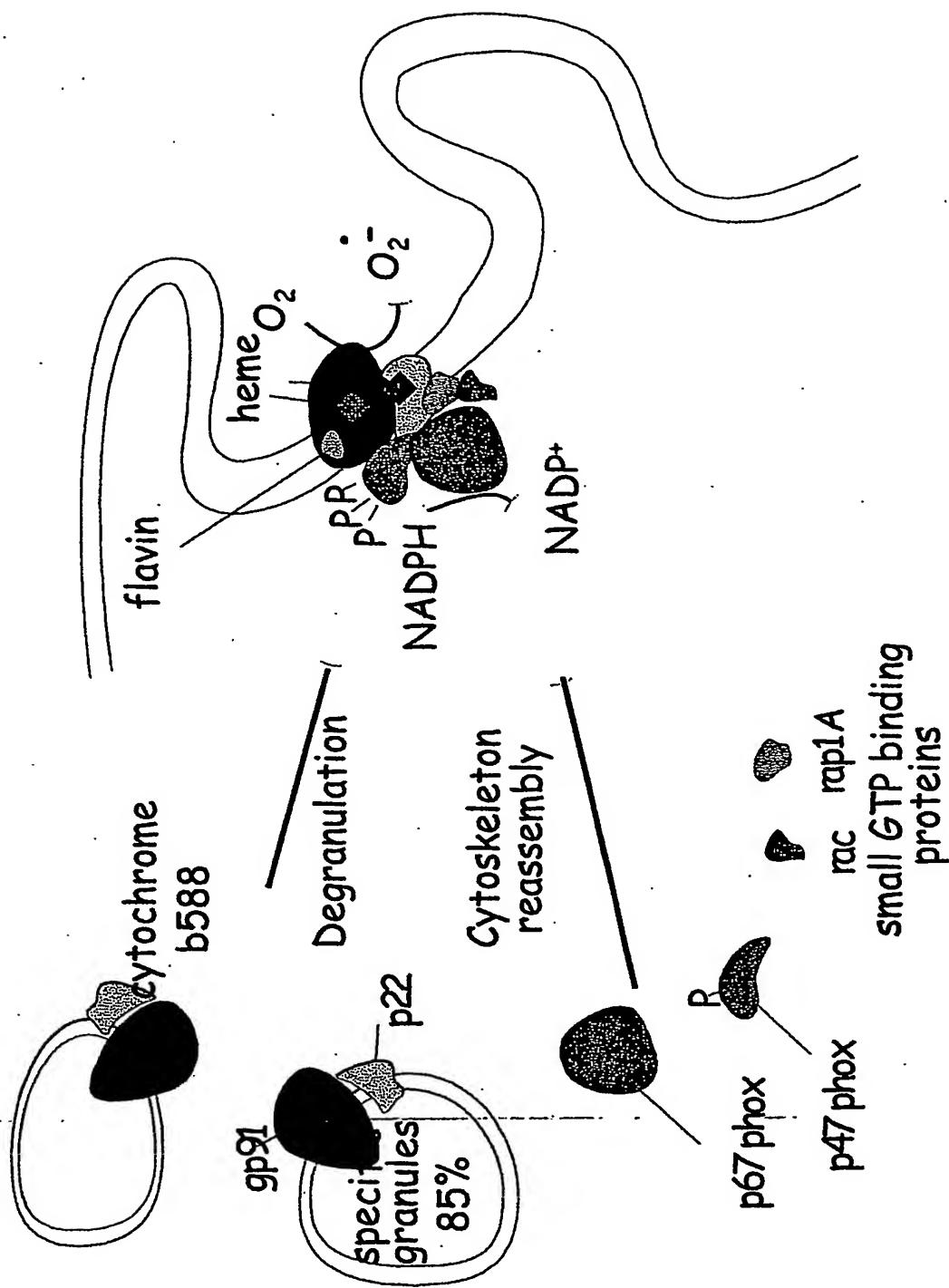


Figure 16

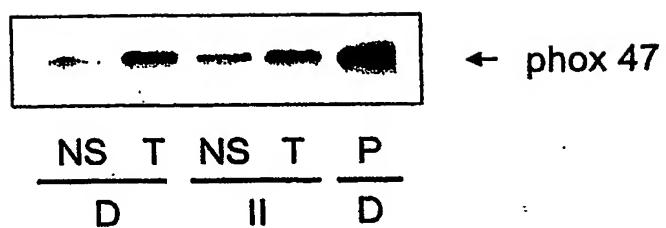


Figure 17

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- BLACK BORDERS
- IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT OR DRAWING
- BLURRED OR ILLEGIBLE TEXT OR DRAWING
- SKEWED/SLANTED IMAGES
- COLOR OR BLACK AND WHITE PHOTOGRAPHS
- GRAY SCALE DOCUMENTS
- LINES OR MARKS ON ORIGINAL DOCUMENT
- REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.